

1           1. A method for diagnosing a malignant neoplasm in a  
2 mammal, comprising contacting a bodily fluid from said  
3 mammal with an antibody which binds to an human aspartyl  
4 (asparaginy) beta-hydroxylase (HAAH) polypeptide under  
5 conditions sufficient to form an antigen-antibody complex  
6 and detecting the antigen-antibody complex.

1           2. The method of claim 1, wherein said neoplasm is  
2 derived from endodermal tissue.

1           3. The method of claim 1, wherein said neoplasm is  
2 selected from the group consisting of colon cancer, breast  
3 cancer, pancreatic cancer, liver cancer, and cancer of the  
4 bile ducts.

1           4. The method of claim 1, wherein said neoplasm is  
2 a cancer of the central nervous system (CNS).

1           5. The method of claim 1, wherein said bodily fluid  
2 is selected from the group consisting of a CNS-derived  
3 bodily fluid, blood, serum, urine, saliva, sputum, lung  
4 effusion, and ascites fluid.

1           6. The method of claim 1, wherein said antibody is a  
2 monoclonal antibody.

1           7. The method of claim 6, wherein said monoclonal  
2 antibody is FB50.

1           8. The method of claim 6, wherein said monoclonal  
2 antibody is selected from the group consisting of 5C7, 5E9,  
3 19B, 48A, 74A, 78A, 86A.

1           9. A method for prognosis of a malignant neoplasm  
2 of a mammal, comprising  
3           (a) contacting a bodily fluid from said mammal  
4 with an antibody which binds to an HAAH polypeptide under  
5 conditions sufficient to form an antigen-antibody complex  
6 and detecting the antigen-antibody complex;  
7           (b) quantitating the amount of complex to  
8 determine the level of HAAH in said fluid; and  
9           (c) comparing the level of HAAH in said fluid  
10 with a normal control level of HAAH, wherein increasing  
11 levels of HAAH over time indicates an adverse prognosis.

1           10. A method of inhibiting tumor growth in a mammal  
2 comprising administering to said mammal a compound which  
3 inhibits expression of HAAH.

1           11. The method of claim 10, wherein said compound is  
2 a HAAH antisense nucleic acid.

1           12. The method of claim 10, wherein said compound  
2 is a ribozyme.

1           13. The method of claim 10, wherein said tumor is  
2 derived from endodermal tissue.

1           14. The method of claim 10, wherein said tumor is  
2 selected from the group consisting of colon cancer, breast  
3 cancer, pancreatic cancer, liver cancer, and cancer of the  
4 bile ducts.

1           15. The method of claim 10, wherein said tumor is a  
2 CNS tumor.

16. A method of inhibiting tumor growth in a mammal comprising administering to said mammal a compound which inhibits an enzymatic activity of HAAH.

17. The method of claim 16, wherein said enzymatic activity is hydroxylase activity.

18. The method of claim 16, wherein said compound is a dominant negative mutant of HAAH.

19. The method of claim 18, wherein said dominant negative mutant HAAH comprises a mutation in a catalytic domain of HAAH.

20. The method of claim 16, wherein said compound is an HAAH-specific intrabody.

21. The method of claim 16, wherein said compound is L-mimosine.

22. The method of claim 16, wherein said compound is a hydroxypyridone.

23. A method of inhibiting tumor growth in a mammal comprising administering to said mammal a compound which inhibits signal transduction through the IRS signal transduction pathway.

24. The method of claim 23, wherein said compound inhibits IRS phosphorylation.

25. The method of claim 23, wherein said compound inhibits binding of Fos or Jun to an HAAH promoter sequence.

1           26. A method of inhibiting tumor growth in a mammal  
2 comprising administering to said mammal a compound which  
3 inhibits HAAH hydroxylation of a NOTCH polypeptide.

1           27. The method of claim 26, wherein said compound  
2 inhibits hydroxylation of an EGF-like repeat sequence in a  
3 NOTCH polypeptide.

1           28. A method of killing a tumor cell comprising  
2 contacting said tumor cell with cytotoxic agent linked to an  
3 HAAH-specific antibody.

1           29. A monoclonal antibody that binds to an epitope  
2 of HAAH.

1           30. The antibody of claim 29, wherein said epitope  
2 is within a catalytic site of HAAH.

1           31. The antibody of claim 29, wherein said  
2 monoclonal antibody is selected from the group consisting of  
3 5C7, 5E9, 19B, 48A, 74A, 78A, 86A.

1           32. The antibody of claim 29, wherein said  
2 monoclonal antibody is selected from the group consisting of  
3 HA238A, HA221, HA239, HA241, HA329, or HA355.

1           33. A composition comprising a monoclonal antibody  
2 that binds to an epitope of HAAH linked to a cytotoxic  
3 agent, wherein said composition preferentially kills tumor  
4 cells compared to non-tumor cells.

1           34. A kit for diagnosis of a tumor in a mammal,  
2 comprising the antibody of claim 29.

1           35. The kit of claim 34, wherein said antibody is  
2 immobilized on a solid phase.

1           36. The kit of claim 35, wherein said solid phase  
2 is selected from a group consisting of an assay plate, an  
3 assay well, a nitrocellulose membrane, a bead, a dipstick,  
4 and a component of an elution column.

1           37. A method of determining whether a candidate  
2 compound inhibits HAAH enzymatic activity, comprising  
3           (a) providing a HAAH polypeptide;  
4           (b) providing a polypeptide comprising an EGF-like  
5 domain;  
6           (c) contacting said HAAH polypeptide or said NOTCH  
7 polypeptide with said candidate compound;  
8           (d) determining hydroxylation of said polypeptide of  
9 step (b), wherein a decrease in hydroxylation in the  
10 presence of said candidate compound compared to that in the  
11 absence of said compound indicates that said compound  
12 inhibits HAAH enzymatic activity.

1           38. A method of determining whether a candidate  
2 compound inhibits HAAH activation of NOTCH, comprising  
3           (a) providing a cell expressing HAAH;  
4           (b) contacting said cell with a candidate compound;  
5 and  
6           (c) measuring translocation of activated NOTCH to  
7 the nucleus of said cell, wherein a decrease in  
8 translocation in the presence of said compound compared to  
9 that in the absence of said compound indicates that said  
10 compound HAAH activation of NOTCH.